REMARKS

Upon entry of this Amendment, Claims 1 – 6, 9 – 14, 16 – 17, 22 – 27, 30 – 36, and 39 – 50[1] will be pending. Claims 10 – 12, 16, 34, and 40-41 are hereby amended. Support for the claim amendments and the new claim may be found throughout the Specification as filed, for example, at the Specification at page 9, lines 3 – 7 and page 36, line 11 – page 37, line 1.

Entry and consideration of the remarks and amendments to Claims 10 – 12, 16, 34, and 40-41 is earnestly solicited. Specifically, consistent with the Examiner's direction, Applicants respectfully submit that Claims 16 and 34 overcome the claim objections and 5, 6, 9 – 12, and 40 – 41 overcome the rejections under at least 35 U.S.C. 112, first paragraph.

I. Advisory Action

Applicants acknowledge the Examiner's Advisory Action dated August 9, 2010. Applicants note that the Examiner indicated that the "proposed amendment introduces new subject matter into claims 10 – 12 and 40 – 41." Advisory Action at page 2. Applicants respectfully disagree, but have submitted a Request for Continued Examination solely in order to facilitate prosecution. Accordingly, Applicants respectfully request entry and consideration of the enclosed claims and remarks.

II. Claim Objections

Applicants thank the Examiner for withdrawing the objections to Claims 1, 16, 17, 22, and 46.

Consistent with the Examiner's suggestion, Applicants have amended Claim 16 by adding a period at the end of the claim. Moreover, per the Examiner's suggestion, Applicants have replaced "*pjlA*, *pjlB*" with "*pflA*, *pflB*" in Claim 34. As such, Applicants respectfully assert that the claim objections are hereby rendered moot.

III. Rejection under 35 U.S.C. § 112, Second Paragraph

[1] Applicants note that the Examiner did not acknowledge entry of Claim 50 in the Final Office Action dated April 30, 2010. Applicants respectfully request an acknowledgment regarding the entry and examination of Claim 50.

Applicants thank the Examiner for withdrawing the 35 U.S.C. § 112, second paragraph, rejection over Claims 1-14, 16-17, 26-29, and 32-49. Final Office Action at pages 3 – 4.

IV. Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-6, 9-14, 16-17, 22-27, 30-36, and 39-49 stand rejected under 35 U.S.C. § 112, first paragraph, written description as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Final Office Action at page 4. Applicants respectfully disagree.

As a basis for the 35 U.S.C. § 112, first paragraph, written description, rejection, the Examiner asserts that "the specification fails to disclose" the following (Final Office Action at pages 5-6):

(1) the structure of *tpiA, gloA, aldA, aldB, IdhA, pflA, pflB, adhE,* and/or *edd,* genes in non-*E. coli*,

(2) the structure of genes encoding enzymes that favor the metabolism of pyruvate to actetate, acetyl-CoA and NADH; and

(3) the structure of genes encoding an enzymes that are involved in the conversion of acetyl-CoA and acetate into acetone.

1. One of ordinary skill in the art would recognize that Applicants were in possession of the claimed subject matter at the time of filing

Given the teachings of the Specification, one of ordinary skill in the art would recognize that Applicants were in possession of the claimed subject matter. Specifically, based on at least the methodology set forth in the Specification, one of ordinary skill in the art would recognize that Applicants were in possession of a sufficient number of strains as well as distinct genes as to satisfy the written description requirement under 35 U.S.C. § 112, first paragraph. For example, in addition to specifically describing numerous genes associated with *E coli*, one of skill in the art would appreciate that the Specification also provides a framework by which to perform the claimed methodology on non-*E coli* genes. Additionally, the Specification provides for other strains capable of being practiced with the invention, for example, *Aspergfflus sp., Bacfflus sp., Brevibacterium sp., Clostridium sp., Corynebacterium sp., Escherichia sp., Gluconobacter sp.,*

Pseudomonas sp., Rhodococcus sp., Saccharomyces sp., Streptomyces sp., Xanthomonas sp., Candida sp, Corynebactedum, C. glutamicum, Saccharomyces, and *S. cerevisiae.* Specification, for example, at page 6, line 28 – page 7, line 5. Accordingly, one of skill in the art would recognize that Applicants were in possession of the claimed invention.

2. Given the teachings of the Specification, one of ordinary skill in the art would have the ability to identify sequences by utilizing specialized databases, such as BLAST, GENBANK, CLUSTALW, and MULTALIN

Moreover, given the teaching of the Specification, one of ordinary skill in the art would have the ability to identify the structure of a wide range of corresponding genes in organisms outside of *E Coli.* Specification, for example, at page 7, lines 6 – 30 and page 10, lines 18 – 27. For example, as set forth in the Specification, one of ordinary skill in the art would have the ability to identify sequences through a percent identity analysis by utilizing one of several disclosed programs, such as BLAST (http://www.ncbi.nlm.nih.gov/BLAST/), CLUSTALW (http://www.ebi.ac.uk/clustalw/), or MULTALIN (http://prodes.toulouse.in ra Jr/mu Italin/cg i-bin/mu Italin.p1). *Id.* at page 7, lines 13 – 20. Each of these databases was described in the Specification as originally filed. As set forth in the Specification, such techniques "are well known in the art and are described, for example, in Sambrook et al. (1989 Molecular cloning: a laboratory manual. 2nd Ed. Cold Spring Harbor Lab., Cold 30 Spring Harbor, New York.)." *Id.* at page 7, lines 27 – 30.

For at least the above reasons, one of ordinary skill in the art would recognize that Applicants were in possession of the claimed invention at the time of filing.

3. The 35 U.S.C. § 112, first paragraph, rejections of Claims 5, 6, 9 – 12, and 40 – 41 are rendered moot by the claim amendments

Applicants respectfully disagree with the rejections of Claims 5, 6, 9 – 12, and 40 – 41, but have amended the claims solely in order to facilitate prosecution. Regarding the Examiner's rejection on the basis of grounds (2) and (3) above, Applicants note that this claim language has been previously modified. Specifically, with respect to (2), the phrase "enzymes that favors the metabolism of pyruvate to acetate" was changed to "pyruvate dehydrogenase complex" in Claims 5, 6, and 9 in the Response filed on January 22, 2010. Regarding basis (3), Applicants

have amended Claims 10 – 12 and 40 – 41 to replace "coding for one or more enzymes involved in the conversion of acetyl-CoA and acetate into acetone" with "genes *adc*, *ctfA* and *B*, *and thl*." Support for this claim amendment may be found in the Specification, for example, at page 9, lines 3 – 7 and page 36, line 11 – page 37, line 1. As such, the rejection of the claims under at least (2) and (3) of 35 U.S.C. § 112, first paragraph, written description is rendered moot and withdrawal of the rejection is respectfully requested.

V. Rejection under 35 U.S.C. § 102(b)

Applicants thank the Examiner for withdrawing the 35 U.S.C. § 102(b) rejection of Claims 1-3, 5-9, 13-14, 16, 22-24, 26- 33, 35-39, and 42-43 over US Patent No. 6,303,352 ("Cameron *et al.*").

VI. Rejection under 35 U.S.C. § 103(a)

Claims 1-2, 5-6, 9-14, 16, 22-24, 26-27, 30-32, 35-36, 39-46, and 48-51[2] stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,303,352 ("Cameron *et al.*") in view of *Biotechnol. Prog.* 16: pages 940-946 (2000) ("Altaras *et al.*") and further in view of *Appl Environ Microbiol.* Mar; 64(3):pages 1079-85 (1998) ("Bermejo *et al.*"). Applicants respectfully disagree.

1. Cameron *et al.* does not teach or suggest an "evolved" strain, let alone an evolved gene exhibiting improved 1,2-propanediol synthase activity

In rejecting the claims, the Examiner states that Cameron *et al.* "discloses a method of modifying or 'evolving' *E. coli* to increase production of 1,2-propanediol by deleting its *tpiA* and/or *gloA* genes and over-expressing genes encoding enzymes that increases metabolism of pyruvate to acetate and/or pyruvate to acetylCoA and NADH." Final Office Action at pages 11 – 12. The Examiner further states that "[t]he difference between the reference of Cameron et al. and the instant invention is that the reference of Cameron et al. does not teach deletion of *IdhaA* and expression of C. *acetobutylicum* gene encoding an enzyme that increases production of acetone." *Id.* at 12. Applicants respectfully dispute the Examiner's characterization of Cameron

[2] Applicants note that there is no pending Claim 51.

et al.

Cameron *et al.* fails to teach any one of steps (b) – (d) of independent Claim 1. Cameron *et al.* does not even mention "evolving" or "evolved" strains or micro-organisms. Moreover, Cameron *et al.* does not teach or suggest any "evolution" process, let alone specific culture conditions that allow for the evolution of endogenous genes in the initial strain. Rather, Cameron *et al.* teach methods of producing 1,2-propanediol by fermentation of sugars by culturing a recombinant microorganism expressing enzymes that catalyze production of 1,2-propanediol in a medium containing a sugar carbon source other than a 6-deoxyhexose sugar. Cameron *et al.*, for example, at page 2, column 2, lines 53 – 56. By utilizing a recombinant microorganism to catalyze production of 1,2-propanediol, Cameron *et al.* actually teaches away from the claims. That is, one of ordinary skill in the art would recognize that there would be no need to conduct at least method steps (b) – (d) of Claim 1 and prepare an "evolved" strain given the recombinant microorganism starting material.

Additionally, unlike Cameron *et al.*, the initial strain of Claim 1, step (b), can be cultivated under selection pressure in a growth medium, such that the cultivation step may result in a strain with different characteristics from those strains set forth in Cameron *et al.* Given this, one of ordinary skill in the art would understand the selection differences between an "evolved" strain and a strain based on a recombinant organism.

2. As described by Altaras *et al.*, the deletion of *IdhaA* alone is insufficient to generate a strain with enhanced 1,2-propanediol

One of ordinary skill in the art would have no motivation to combine Altaras *et al.* with Cameron *et al.* in a manner that would render the claims obvious. For one, Altaras *et al.* provides no motivation to delete the *IdhaA* gene alone with an expectation that such a deletion would result in enhanced production of 1,2-propanediol. Rather, Altaras *et al.* teaches that the specific overexpression of certain genes in combination with the deletion of other genes may result in enhanced production of 1,2-propanediol. For example, strain NLD294::pNEA35, presents a mutation in *ldhA* gene and also expresses *gldA, mgs* and *fucO* genes. Altaras *et al.* at Table 1 and Table 5. As set forth in Altaras *et al.*, the specific combination of the deletion of *ldhA* together with the overexpression of genes *gldA, mgs* and *fucO* leads to enhanced production of 1,2-propanediol. One of ordinary skill in the art would recognize this and would have no

motivation to delete a *IdhaA* gene alone in a strain of Cameron *et al.* with an enhanced 1,2-propanediol.

In rejecting the claims, the Examiner further states that Bermejo *et al.* "discloses expression of C. *acetobutylicum* gene encoding an enzyme that increases production of acetone in *E. coli* in order to improve solvent production and an acetone producing *E. coli* may be useful hosts, which decreases the accumulation of detrimental acetate (page 936)." Final Office Action at page 12. However, in citing to Bermejo *et al.*, the Examiner provides no motivation as to why one of ordinary skill in the art would simultaneously be motivated to delete of *IdhaA* while at the same time increasing expression of a C. *acetobutylicum* gene. As set forth in Altaras *et al.*, the deletion of *ldhA* together with the overexpression of specific genes, *gldA, mgs* and *fucO*, leads to enhanced production of 1,2-propanediol. None of Cameron *et al.*, Altaras *et al.*, or Bermejo *et al.* teach or suggest that the specific deletion of *IdhaA* together with increased expression of a C. *acetobutylicum* gene would result in a strain with enhanced 1,2-propanediol, let alone a strain with a decreased acetate concentration. In combining these three references in piecemeal fashion, the Examiner has failed to consider the interrelatedness of three distinct methodologies. With this, one of ordinary skill in the art would have no motivation to combine the teachings Cameron *et al.*, Altaras *et al.*, or Bermejo *et al.* with a reasonable expectation of success.

As such, for at least the reasons above, Cameron *et al.* in view of Altaras *et al.* and Bermejo et al. do not render the claims obvious. Accordingly, withdrawal of the rejections is respectfully requested.

CONCLUSION

In view of the amendments and remarks above, Applicants respectfully submit that this application is in condition for allowance and request favorable action thereon. The Examiner is invited to contact the undersigned at (202) 508-3400 if any additional information is required.

Respectfully submitted,

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